Paperless, integrated, validated:

«Increasing productivity with today's best-practice weighing solutions»

Increased Certainty, Consistent Good Quality

The goal: consistent good quality

The way: mixing the right formula

The means: weighing the right components accurately, i.e. within process tolerances

The key: using the right scale

The implication: proving in the production setting that the scale's accuracy can match the tolerances

The solution: determining the scale's measurement uncertainty and defining a proven weighing range, especially the crucial minimum weight

1

Customer Peace of Mind

The certainty: weighing above the minimum weight ensures all measurements are within tolerances, i.e. quality is guaranteed !

The piece of mind: achieving consistent good quality, built into the process and not only detected during final analysis

The piece of mind II: easily passing the next audit or inspection by having documented why and how each scale fits the process requirements

2

The art of making medicine

1. API Synthesis → 2. Dispensing → 3. Mixing → 4. Tableting → 5. Packaging

Agenda

- Increasing Productivity in Dispensing
- Increasing Productivity in Mixing
- Increasing Productivity with connectivities

Dispensing: Where exact amounts count

1. API Synthesis → 2. Dispensing → 3. Mixing → 4. Tableting → 5. Packaging

- Raw material identification
- Raw material weighing

- High Resolution digital scales
- Precision balances XP Line
- Analog scales
- Weighing indicators IND449, IND690, ID30
- Formulation solutions

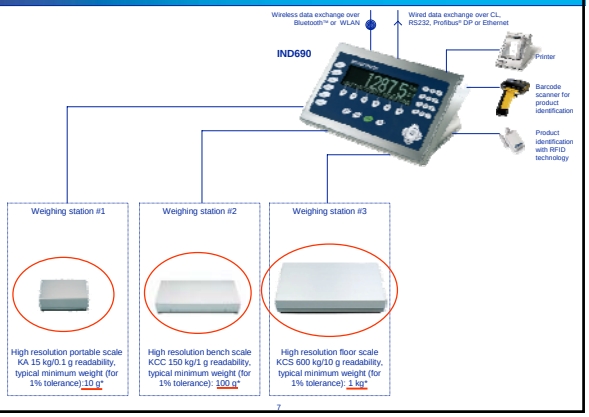
Knowing what scale to use for what process

Who needs to know the minimum weight of a scale?

Anybody who is concerned about quality!

Minimum weight ensures that you use the proper scale for your process and that the weighing results can be trusted. It ensures compliance with quality specifications and prevents bad batches and costly measurement mistakes.

Accuracy over a broad weighing range


Wireless data exchange over Bluetooth™ or WLAN
Wired data exchange over CL, RS232, Profibus® DP or Ethernet
IND690
Printer
Barcode scanner for product identification
Product identification with RFID technology
Weighing station #1
Weighing station #2
Weighing station #3
High resolution portable scale KA 15 kg/0.1 g readability, typical minimum weight (for 1% tolerance): 10 g*
High resolution bench scale KCC 150 kg/1 g readability, typical minimum weight (for 1% tolerance): 100 g*
High resolution floor scale KCS 600 kg/10 g readability, typical minimum weight (for 1% tolerance): 1 kg*

7

A Real Case: Formulation

Weighing Application :

Formulation of 3 compounds A, B and C in a reactor (reactor tare: 40kg)

Compound A: 50.0 ± 2.5kg

Compound B: 28.0 ± 1.0kg

Compound C: 2.00 ± 0.02kg

The weighing **targets** within those **tolerances** must be guaranteed, because the formulation is quality relevant

You wants to use the appropriate scale(s), with the accuracy needed, to the best price.... What is/are scale (s) that fit to your need ?

8

Is the minimum weight the same as the readability ?

No

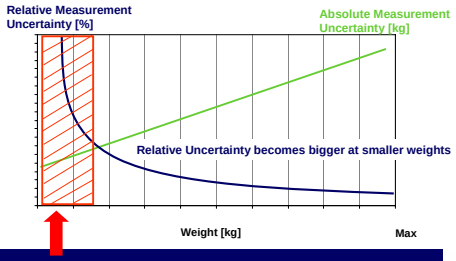
Readability is just the smallest discernible mass difference and can be electronically adjusted to whatever value !

The minimum weight depends on the repeatability of the scale and other factors that sum up in the **MEASUREMENT UNCERTAINTY**.

9

Measurement Uncertainty

U [kg] = U_0 + Constant x Weight

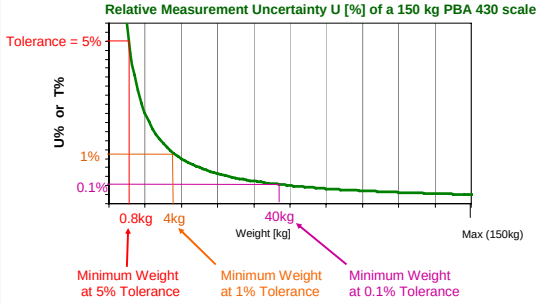


For very small weights, the **relative measurement uncertainty** can be so high that the weight cannot be trusted anymore!

10

Finding the right Minimum Weight

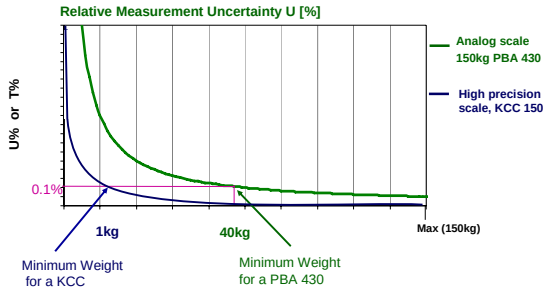
Relative Measurement Uncertainty U [%] of a 150 kg PBA 430 scale



The **minimum weight** is the lower weight limit for a scale, below which the **relative measurement uncertainty** is larger than the acceptable weighing **tolerance**

11

Comparing different scales



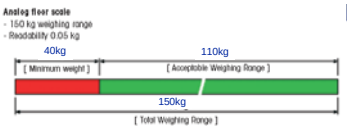
For the same tolerance of 0.1% the K-line having a minimum weight of 1kg is 40 times better than the PBA 430 !

12

Minimum Weight for 2 different scales

For a tolerance of 0.1%:

Analog scale
150kg PBA 430



High precision scale
KCC 150

Determination of the minimum weight of a scale ensures that all measurements are within tolerances !

Uff, that was a lot of theory !

Let us see how we can make money out of it!

14

15

From Minimum Weight to MinWeigh

- **MinWeigh®** is an application created and trademarked by METTLER TOLEDO
- MinWeigh assures that weighments are within the required tolerances of a process. This is the case when the customer weighs above the minimum weight threshold.
- The minimum weight is documented by a MinWeigh certificate.
- The minimum weight is entered into the terminal and the MinWeigh warning function is activated by the technician.

16

MinWeigh Warning Function

As long as the net weight is below the defined minimum weight the MinWeigh function of the IND 690 warns the operator by displaying or flashing this symbol

17

MinWeigh Warning Function

On the IND 4x9 and the older IND 560 the symbol is an asterisk (*)

Note: The minimum weight is independent of tare

18

MinWeigh Recalculation Capability

As tolerances may change from process to process, the minimum weight can be recomputed easily.

Just enter a new tolerance value and/or safety factor and the terminal uses the stored U to recalculate the new minimum weight.

560

690

780

19

Recommendations & Benefits

Beware that…

- These estimated values do never replace an actual determination of the minimum weight.

  This has to be made at the location of the weighing system under real working conditions.

However…

- The estimation of the minimum weight is a powerful tool to help you select the right scale for the application.

20

“MinWeigh helped us get consistent batch quality”

„Since we determined the measurement uncertainty and identified MinWeigh on all scales in our plant, we have not had an out-of-specification batch anymore because of misweighments.

Before that, more than once I observed operators weighing 1.0kg of a catalyst on the 3000kg scale, because it felt more comfortable for them than using a smaller scale. And they even got a stable reading from those measurements - however, the error in those weighing processes was huge !

Now with MinWeigh I have a scientific way to explain accuracy, measurement uncertainty and weighing errors to the operators as well as the quality managers and auditors.

What is great is that the scales now warn the operators when they want to use an inadequate scale and weigh below the certified MinWeigh.

The implementation of MinWeigh was a tremendous step forward in our quality system.“

21

Weighing in the dispensing room

Dispensing: Lay-out & Installation

Precise and safe in an ex-proof environment! , Above or Pit ???

Ex

Zone 2 or Zone 1

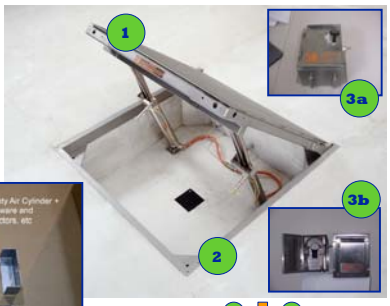
1. Dispensing → 2. Mixing → 3. Tableting → 4. Packaging

23

Filling Application - Pharma

24

Sanitary Cleaning EZ–Clean



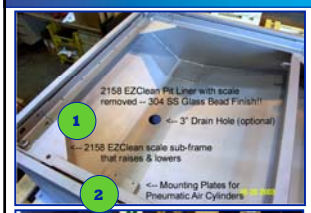
Pneumatic Cylinder Assembly including the Safety Air Cylinder + Self-Deploying Mechanical Locking Hardware and Base Mounting Hardware and "T" connectors, etc

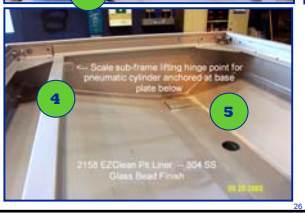
EZ-Clean Orders 1 + 2

1. **Select Scale with Harsh or Panel Mount Enclosure** (Scale Frame NOT included)
2. **Select Standard Pit Frame or Pit Liner**

25

EZ-Clean Pit Liner Components


2158 EZClean Pit Liner with scale removed -- 304 SS Glass Bead Finish!!
1
<-- 3" Drain Hole (optional)
<-- 2158 EZClean scale sub-frame that raises & lowers
2
<-- Mounting Plates for Pneumatic Air Cylinders


<-- Scale sub-frame lifting hinge point for pneumatic cylinder anchored at base plate below
4
5
2158 EZClean Pit Liner -- 304 SS Glass Bead Finish

26

EZ-Clean Pit Liner Installation

2158 EZClean Pit Liner resting in 'rough opening" cut-out via brackets -- ready for pouring of concrete!!

2158 EZClean Scale resting in "rough opening" cut out
NOTE: conduit run out of back end to wall

27

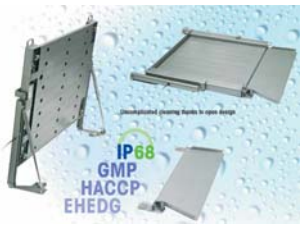
EZ-Clean Pit Liner Installation

28

Finished Product

29

Above Ground installation.



30

Agenda

- Increasing Productivity in Dispensing
- Increasing Productivity in Mixing
- Increasing Productivity with connectivities

Pharmaceutical Preparations Processes

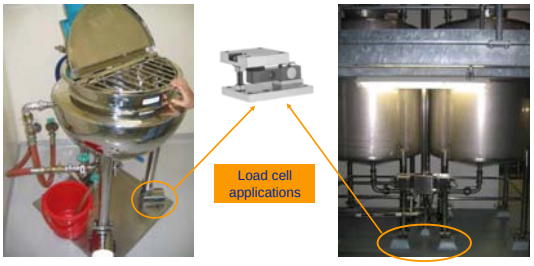
Pharmaceutical processes: from API to market

1. Dispensing	2. Mixing	3. Tableting	4. Packaging
Raw material identification	Granulates / Pellets making	Tablet pressing / Encapsulation	Packaging / Bottling
Raw material weighing	Sieving and Drying	Metal detection	Final inspection
	Mixing of API with excipients	In-process quality control	

32

Applications for Mixing

Bringing the ingredients together: mixing the right amount!



1. Dispensing → 2. Mixing → 3. Tableting → 4. Packaging

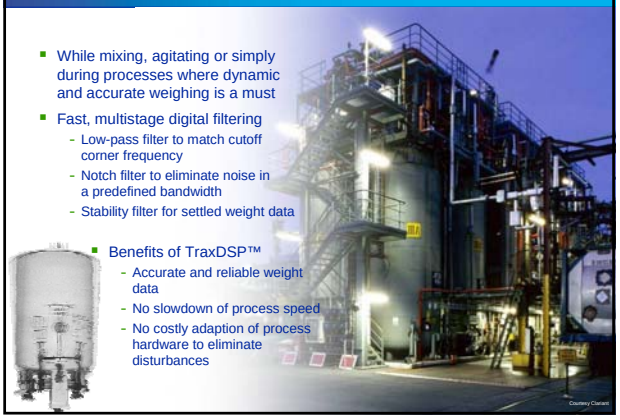
33

Predictive maintenance TraxEMT

- Schedules and tracks its own maintenance
- Predicts load cell failures before they occur
- Alerts designated individuals by eMail, SMS or over any data interface to a DCS
- Performs fault recognition and recovery (run-flat estimation) in case a load cell fails.

Digital filtering TraxDSP™

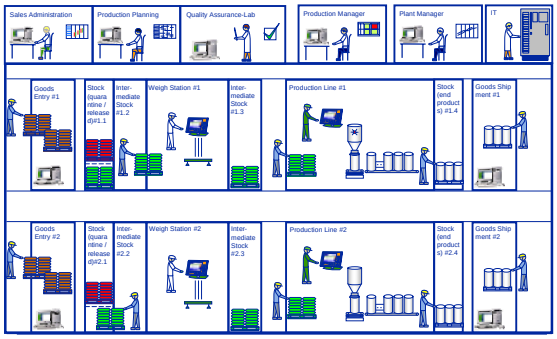
- While mixing, agitating or simply during processes where dynamic and accurate weighing is a must
- Fast, multistage digital filtering
  - Low-pass filter to match cutoff corner frequency
  - Notch filter to eliminate noise in a predefined bandwidth
  - Stability filter for settled weight data
- Benefits of TraxDSP™
  - Accurate and reliable weight data
  - No slowdown of process speed
  - No costly adaption of process hardware to eliminate disturbances



Agenda

- Increasing Productivity in Dispensing
- Increasing Productivity in Mixing
- Increasing Productivity with connectivities

Formulation Basics – Material- and Workflow



37

Manufacturing Pharmaceutical Preparations

Consist of:

- Recipe-based production
- Manual dispensing
- Comply with GMP
- → Validated processes with full documentation

Improvement options:

→ Computer-based systems can help to better document production batches (every single step is documented!)

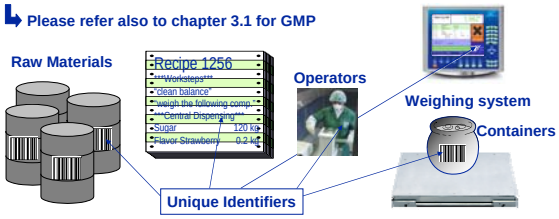
- **Recipe Management**
- **Standard Reports**
- **Tracking with Labels**

38

GMP Compliance

- Performance of Equipment Qualification (EQ) by determining
  - The right accuracy for weighing processes
  - The measurement uncertainty and minimum weight determination
- System validation for software and for production processes
- Cleaning validation procedure avoiding X-contamination
- Unequivocal material identification

Please refer also to chapter 3.1 for GMP



39

Potential Errors and Improvement Options - I

- Wrong material picked from stock
- Wrong material dispensed
- Material with wrong quality status used
- Expired material dispensed
- Dispensed amount out of tolerance (tolerances not considered)

Improvement options with a computer-based system are:

- Pick-list guides operator in warehouse
- Unique Material identification with Bar Code Reader (BCR)
- Batch data easily checked with one scan
- Check of production terminal completeness
- Deviation management can assure tolerances

40

Potential Errors and Improvement Options - II

- Material is dispensed into wrong bin
- Weighing system are not properly calibrated (doubtful mixtures/end products)
- Wrong balances are used (necessary accuracy not considered)
- Production batch is not defined (no recall possible later on)
- Material is not identified after weighing (potential mistake in mixing / production area later on)

All above mentioned possible errors lead to → end product quality out of specification → batch rework and **higher production costs!**

Improvement options with a computer-based system are:

- Container management
- Calibration routine
- Only the use of the most suitable scale is allowed by the system. All unsuitable scales are excluded!
- Check for production completeness

41

Key Benefit: Profitability / Costs

Profitability / Costs

- 4 eyes principle not needed with computer based formulation system
  → COST OPTIMIZATION (reduction human resources)
- Cut down material- and batch wastage due to controlled dispensing (computer based system including target weight with tolerances)
  → PROFITABILITY INCREASE
- Number of bad batches, where rework has to be done can be reduced
  → EFFICIENCY INCREASE in production (throughput)
- Using a standard formulation solution
  → EASY to STANDARDIZE and ROLE-OUT SYSTEM-SOLUTIONS to other plants or internationally

42

Key Benefit: Ensuring Product Quality

Ensuring product quality

- Operator is securely guided through recipe structure
  → HUMAN ERRORS reduced
  → Reduction of material wastage and wrong mixtures
- Reduction of wrong mixtures and less waist means additionally
  → LESS REWORK
  → reproducible and consistent quality
- → Number of bad batches and the loss of valuable materials is reduced tremendously

43

Key Benefit: Increase Productivity

Increase productivity

- Operator is guided step by step through the formulation process
  → Improve PRODUCTION ACCURACY
- Due to simple and user friendly screen layouts instructions can be followed easily and fast
  → PRODUCTIVITY INCREASE
- After a short product training the operators can work with the formulation system comfortably
- ROI calculation examples show a payback period of just a few months!
- After pay-back-period the money and resource savings continue and quality can be reproduced on a much more stable basis because of the computer based system

44

Key Benefit: Ready for 21CFR Part 11

Ready to comply with 21CFR Part 11

- FormWeigh.Net is designed to comply with 21CFR Part11 requirements
- Regulations compliant production (21CFR Part11, EN 178/2002)
  → AUDIT EFFORTS reduction
  → FULLY ELECTRONICALLY DOCUMENTED PROCESSES
- Due to fully documented processes tracing back in case of an unforeseen event is very easy
  → IMPROVE TRACKING and TRACING capabilities
  → FASTER REACTION possible
  → Easier to HANDLE DEVIATIONS

45

Key Benefit: Easy Integration with ERP

Easy integration with ERP system

- Seamless integration allows trouble free data transfer from ERP- or MES systems to Formweigh.Net
  → ELIMINATION of MANUAL DATA ENTRY
  → PAPERLESS PRODUCTION and ORDER GENERATION
  → LESS DATA-TYPISTS
  → REDUCTION MISSTYPINGS → PRODUCTION ERRORS
  → NO REDUNDANT DATA in different systems
- Due to standard interface, customizing can be done instead of programming
  → SHORT IMPLEMENTATION-, PROJECT TIME
- Data availability on key stroke
  → IMPROVE PROCESS TRANSPARENCY
  → DECISION BASE improvement due to this fast data collection
- Higher integration (processes centralization
  → master data and order generation at one place)

46

Software & Connectivity - Summary

Improvements:

- Cost optimization
- Profitability increase
- Efficiency increase
- Eliminate human errors → wrong mixtures, batch rework & wastage of valuable material reduction
- paperless production 21CFR Part11, EN 178/2002 compliant production
- Reproducible and consistent quality due to…
  - ✓ Material identification by using Bar Code Reader
  - ✓ Fully documented processes
  - ✓ Seamless integration

Handwritten identification | Lost identification | Manual documentation

47

Q & A

«With METTLER TOLEDO you can increase productivity with today‘s best-practice GMP weighing solutions»